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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/565,327

01/20/2006

Hideaki Imamura

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EXAMINER

BLAND, LAYLA D

ART UNIT

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/565,327	<b>Applicant(s)</b> IMAMURA ET AL.	
	<b>Examiner</b> LAYLA BLAND	<b>Art Unit</b> 1623	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 07 February 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) 3-8 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 9-12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>8/7/2006</u> .  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

Applicant's election without traverse of Group I, claims 1-5 and 9-12 and the species 3, which corresponds to formula (II) in claim 2, in the reply filed on February 7, 2008, is acknowledged. The elected species is a free base and not a salt, solvate, or hydrate; thus claims 3-5 are withdrawn from consideration at this time. Claims 1-12 are pending. Claims 3-5 and 6-8 are withdrawn from consideration as being drawn to a non-elected invention. Claims 1, 2, and 9-12 are examined on the merits herein.

### ***Priority***

This application is a national stage entry of International Application No. PCT/JP04/10741, filed July 21, 2004, which claims priority to Application No. PCT/JP03/09393, filed on July 24, 2003. The copy of certified copy of the priority has been filed with the instant Application. It is noted that Application No. PCT/JP03/09393 is in Japanese; no translation of said application into English has been provided.

### ***Drawings***

The subject matter of this application admits of illustration by a drawing to facilitate understanding of the invention. Pages 14 and 15 of the specification include a brief description of the drawings, but no drawings are present. Applicant is required to furnish a drawing under 37 CFR 1.81(c). No new matter may be introduced in the required drawing. Each drawing sheet submitted after the filing date of an application

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must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d).

### ***Claim Objections***

Claim 11 is objected to because of the following informalities: the claim lacks a period. Additionally, the claim recites "using" which perhaps should read "comprising." Appropriate correction or clarification is required.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, and 9-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for crystalline compounds of formula (I) and salts thereof, does not reasonably provide enablement for solvates thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in *Wands* states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not

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be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention.

"Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

*(1) The nature of the invention and (2) the breadth of the claims:*

The claims are drawn to compounds of Formula I, salts and solvates thereof. Thus, the claims taken together with the specification imply that any and all solvates of all the compounds encompassed by Formula I are claimed.

*(3) The state of the prior art and (4) the predictability or unpredictability of the art:*

Vippagunta et al. (*Advanced Drug Delivery Reviews* 48 (2001) 3-26) teach that predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice of a compound is complex and difficult. Certain molecular shapes and features favor the formulation of crystals without solvent. No computer programs are currently available for predicting

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the crystal structures of hydrates and solvates and generalizations cannot be made for a series of related compounds. [page 18, 3.4]

*(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:*

The specification has provided guidance for the synthesis of crystalline compounds of Formula I but not for the synthesis of solvates of compounds of Formula I. On page 23 of the specification, Example 5, compound 5 is drawn as an ethanol solvate and the example cites residual ethanol of 5.49%. However, no crystal structure for the solvate is provided and residual ethanol is not evidence of solvate formation. Furthermore, even if guidance for the production of compound 5 was given, Vippagunta et al. teach that generalizations cannot be made for a series of related compounds; thus formation of one solvate would not support enablement for the others.

*(8) The quantity of experimentation necessary:*

Considering the state of the art as discussed by the references above, particularly with regards to the teaching of Vippagunta et al. and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to make the invention commensurate in the scope of the claims.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Kojiri et al. (English translation of JP 10-245390, PTO-1449 submitted August 7, 2006).

Kojiri et al. teach injection of antitumor compounds, including the compound made in Example 14 [page 8, lines 5-17 and Table 1]. The compound of Example 14 [page 21, Example 14] has the same structural formula as the elected species in the instant application. Although claims 9-12 are drawn to pharmaceutical compositions or agents comprising crystalline formula (I) and Kojiri et al. do not teach a crystalline compound, the injectable composition taught by Kojiri et al. is a solution. A solution made from a crystalline compound is the same as a solution made from the corresponding amorphous compound. Thus, the composition taught by Kojiri et al. anticipates claims 9-12, which are drawn to compositions or agents for injection which can comprise solvents.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kojiri et al. (English translation of JP 10-245390, PTO-1449 submitted August 7, 2006).

Kojiri et al. teach compound 25, which has the same structural formula as the elected species in the instant application [page 21, Example 14]. This compound and others prepared by Kojiri et al. can be purified by methods known in the field of organic chemistry, including recrystallization [0021].

Kojiri et al. do not teach crystalline compound 25.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare a crystalline form of compound 25, taught by Kojiri et al. The skilled artisan would have been motivated to do so because Kojiri et al. suggest purification by recrystallization. The skilled artisan would have had a reasonable expectation of success because recrystallization is a technique which is well known for purification of organic compounds, and could be accomplished by routine experimentation.

It is noted that the instant specification states that compounds prepared by the method of Kojiri et al. are amorphous. For this reason, claims 1 and 2 are not anticipated by Kojiri et al.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAYLA BLAND whose telephone number is (571)272-9572. The examiner can normally be reached on M-F 9:00-5:00.



If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Layla Bland/  
Examiner, Art Unit 1623

/Shaojia Anna Jiang, Ph.D./

Supervisory Patent Examiner, Art Unit 1623